Cardiac vomiting

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This survey was stimulated by a recent article on vomiting as a diagnostic aid in acute cardiac ischaemia in which the incidence of vomiting in 109 consecutive coronary care unit patients was prospectively related to the nature and site of infarction.¹

In transmural infarction, about half the patients had vomited, even before the use of analgesic drugs. This high incidence was not seen in subendocardial infarction and the authors concluded that "the vomiting reflex, if such exists, might arise as a consequence of damage to the subpericardial tissue". The authors briefly referred to the possibility of the nausea and autonomic disturbance being related to the Bezold-Jarisch reflex. It may be of interest to review the now extensive physiological data on this subject, which has clinical relevance to many other circulatory disturbances.

History

Albert von Bezold was the Professor of Physiology in Würzburg, an old university city in Southern Germany. The Physiology Institute there has since housed other distinguished physiologists including Adolf Fick of cardiac output fame.

ANIMAL STUDIES

Von Bezold and a student Hirt² were working on the reflex circulatory effects of the alkaloids of Mistletoe and Hellebore, newly isolated by two French chemists, Pelletier and Cavantou. In a series of beautifully executed experiments they showed that the vascular and cardiac depression was reflex and blocked by vagotomy. They also suggested that the receptors signalled the pressure in the heart and that the alkaloids stimulated the receptors to produce a continuous discharge which led to bradycardia and arterial dilatation in the mesenteric bed.

About 80 years later Jarisch and his colleagues showed that the receptors appeared to be in the left

ventricle³⁻⁵; Dawes⁶ located them in the distribution of the left coronary artery.

Until this time the reflex had been thought of as a "protective" reflex at times of cardiac insult or damage. I was able to show that the reflex could be elicited in the conscious dog by injections of nicotine through an indwelling catheter into the pericardial sac. These injections caused no apparent discomfort despite profound cardiovascular effects and caused me to question the concept of a protective reflex.^{7,8} Later both Widdicombe and I in Oxford, and Coleridge and his colleagues in Leeds showed that the receptors were mechanoreceptors with unmyelinated ("c"-fibre) axons. They were excited during systole, especially by the vigorous contractions caused by adrenaline, and were not particularly well excited by cardiac distension.⁹⁻¹¹ We felt that they might well signal intramyocardial tension. More recent experiments by Fox's group have confirmed this.¹² They believe that the reflex serves to match the force of contraction of the left ventricle to the peripheral resistance. Thus at times when cardiac output rises, for example during exercise, ventricular emptying is facilitated by the drop in resistance. Abrahamsson and Thoren¹³ made the important observation that stimulation of these ventricular mechanoreceptors led also to reflex gastric dilatation and eventual vomiting. The gastric dilatation was rapidly reversed by local anaesthetic injected into the pericardial sac. The Swedish group also made the important observation that the ventricular receptors had very powerful effects on the renal vascular bed even at low discharge rates.¹⁴ They could thus have a great importance in blood volume control.

STUDIES ON LEFT VENTRICULAR REFLEX IN MAN

It seems very probable that the same reflex operates in man for the following reasons.

(1) Injection of contrast medium into the coronary arteries results in reflex bradycardia and forearm vasodilatation.¹⁵

(2) Derivatives of veratrum such as veriloid were

abandoned in the treatment of hypertension because it proved impossible to separate the desirable hypotension and bradycardia from the undesirable vomiting.

(3) Patients with aortic stenosis (with increased ventricular wall tension) show on exercise an abnormal peripheral vasodilatation in non-exercising muscle. This was not seen with mitral stenosis. It was corrected by aortic valve replacement.¹⁶

(4) Nausea and vomiting (and sometimes syncope) are not uncommon at the end of heavy exercise. At this time sympathetic drive is high but the heart is empty because of the abrupt cessation of venous return from the now quiescent leg muscles. These are exactly the same conditions which we found to excite the receptors in animal studies.^{9,11} This reaction has been notably reduced in athletes by continued jogging and less abrupt cessation of exercise after a race.

(5) The same circumstances (empty heart and reflex tachycardia and sympathetic drive from baroreceptor reflexes) may occur with peripheral venous pooling when standing in hot weather and trigger the simple faint or vasovagal reaction.

Pathophysiology of ventricular receptors in man

(1) MYOCARDIAL INFARCTION

The autonomic disturbances which occur early in myocardial infarction, namely bradycardia, hypotension, and vomiting^{1,17} so closely resemble the effects of stimulation of ventricular receptors in animals that it seems likely that the same mechanisms obtain. Plasma catecholamines are much increased in myocardial infarction and this was found to excite the receptors in animals. It is debatable whether the reflex originates from receptors in the damaged myocardium or in the healthy myocardium. On purely mechanical grounds it might be thought that the wall tension in non-infarcted muscle is likely to be high (and therefore excitatory) since it is subject to a high sympathetic drive while attempting to maintain the cardiac output. The work of Ingram *et al.*¹ in which it was shown that autonomic effects were confined to large transmural infarctions and were equally common in anterior as in inferior infarction might be taken to support this, but there is some indirect evidence that the receptors are more likely to be located in the territory of the coronary artery supplying the inferior wall of the left ventricle.¹⁸ The Belfast work found bradycardia to be more common in inferior (77%) than in anterior infarction (32%).¹⁷ This therefore suggests that the receptors responsible for the reflex autonomic effects are located in the ischaemic muscle. We do know that the receptors can be stimulated by chemicals such as the radio-opaque contrast media. We also know that certain prostaglandins can excite the ventricular receptors.¹⁹ It is therefore quite possible that the ischaemic muscle

itself might release excitatory substances. We need to resolve this with further prospective clinical studies.

(2) SIMPLE VASOVAGAL FAINTING

Vasovagal syncope can occur from central nervous psychologically induced mechanisms or from environmentally triggered mechanisms such as the familiar postural syncope induced by orthostasis. I have suggested above how sympathetic drive to an empty heart might trigger the fainting reaction. Nausea and vomiting frequently accompany simple fainting.

(3) PROSTAGLANDIN ABORTIONS

Vasovagal reactions are sometimes seen during termination of pregnancy by prostaglandins. In animals these substances have been shown to excite the ventricular receptors.

(4) HEART FAILURE

Stimulation of the ventricular receptors increases renal blood flow and urine flow. The failing heart has decreased contractility and the myocardial concentration of noradrenaline is increased. This would lead to decreased stimulation of ventricular receptors which might thus be part of the mechanism for increasing fluid retention in heart failure.

(5) SYNCOPE IN AORTIC STENOSIS

This appears to be triggered from receptors in the left ventricle. Syncope on exercise does not occur in patients with mitral stenosis, where the pressure rise is confined to the left atrium and pulmonary circulation (see above).

(6) HYPOTENSION AND BRADYCARDIA FROM CARDIAC HANDLING

Estrin and his colleagues have shown that the ventricular receptors can be stimulated by mechanical compression of the heart.¹² The reflex cardiovascular depression could be blocked by local anaesthetic in the pericardium.

(7) DIGITALIS-INDUCED BRADYCARDIA

Animal studies have shown that digitalis glycosides excite the left ventricular receptors,²⁰ to cause hypotension and sinus bradycardia. The hypotension lasts longer than with veratridine. The heart rate of patients with cardiac transplants is not slowed by digitalis since the afferent nerves are interrupted.²¹

Conclusion

Left ventricular receptors which appear to signal intramyocardial tension cause bradycardia and vasodilatation, and increase urine flow. They are probably important in blood volume control and in adjusting the

circulation during exercise. When strongly stimulated they cause nausea and reflex vomiting. They may be involved in the autonomic disturbances at the onset of myocardial infarction, syncope in aortic stenosis, vaso-vagal syncope, and fluid retention in heart failure.

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